```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

NEWS  1              Web Page URLs for STN Seminar Schedule - N. America
NEWS  2              "Ask CAS" for self-help around the clock
NEWS  3   May 12     EXTEND option available in structure searching
NEWS  4   May 12     Polymer links for the POLYLINK command completed in REGISTRY
NEWS  5   May 27     New UPM (Update Code Maximum) field for more efficient patent
                     SDIs in CAplus
NEWS  6   May 27     CAplus super roles and document types searchable in REGISTRY
NEWS  7   Jun 28     Additional enzyme-catalyzed reactions added to CASREACT
NEWS  8   Jun 28     ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                     and WATER from CSA now available on STN(R)
NEWS  9   Jul 12     BEILSTEIN enhanced with new display and select options,
                     resulting in a closer connection to BABS
NEWS 10   Jul 30     BEILSTEIN on STN workshop to be held August 24 in conjunction
                     with the 228th ACS National Meeting
NEWS 11   AUG 02     IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                     fields
NEWS 12   AUG 02     CAplus and CA patent records enhanced with European and Japan
                     Patent Office Classifications
NEWS 13   AUG 02     STN User Update to be held August 22 in conjunction with the
                     228th ACS National Meeting
NEWS 14   AUG 02     The Analysis Edition of STN Express with Discover!
                     (Version 7.01 for Windows) now available
NEWS 15   AUG 04     Pricing for the Save Answers for SciFinder Wizard within
                     STN Express with Discover! will change September 1, 2004
NEWS 16   AUG 27     BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 17   AUG 27     BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                     status data from INPADOC
NEWS 18   SEP 01     INPADOC: New family current-awareness alert (SDI) available
NEWS 19   SEP 01     New pricing for the Save Answers for SciFinder Wizard within
                     STN Express with Discover!
NEWS 20   SEP 01     New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 21   SEP 14     STN Patent Forum to be held October 13, 2004, in Iselin, NJ

NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 10:32:23 ON 21 SEP 2004

=> file reg
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
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h eb c g cg b cg eb

FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 10:32:29 ON 21 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2
DICTIONARY FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

=> l1
L1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l1
L1 HAS NO ANSWERS
L1 STR
Cb 17Ak 18

Page 1-A

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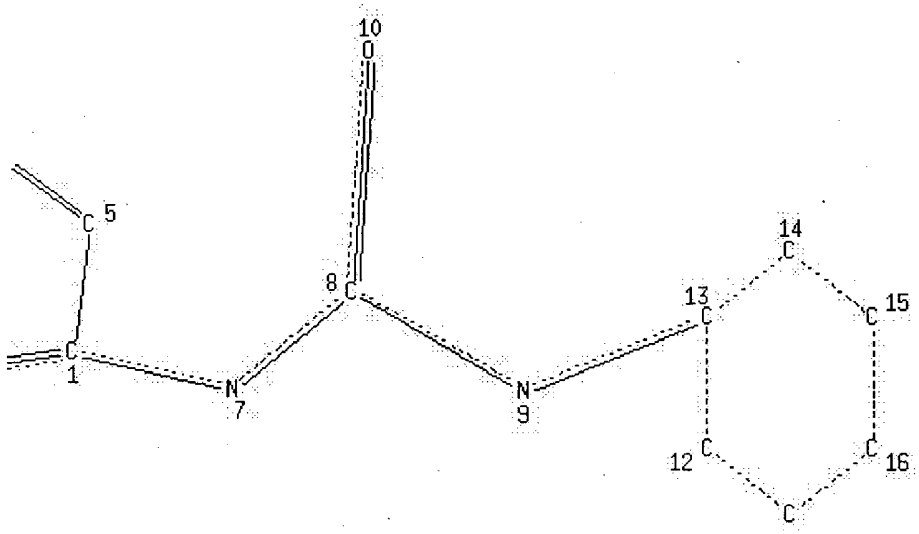

Page 1-B

11

Page 2-B

VAR G1=17/18

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NSPEC IS R AT 3
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MLEVEL IS CLASS AT 7 8 9 10 17 18
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> s 11
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SAMPLE SCREEN SEARCH COMPLETED - 53 TO ITERATE

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 624 TO 1496

h eb c g cg b cg eb

PROJECTED ANSWERS: 173 TO 747

L2 23 SEA SSS SAM L1

=> s l1 full
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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED - 893 TO ITERATE

100.0% PROCESSED 893 ITERATIONS 377 ANSWERS
SEARCH TIME: 00.00.01

L3 377 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 156.68 156.89

FILE 'HCAPLUS' ENTERED AT 10:34:46 ON 21 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 21 Sep 2004 VOL 141 ISS 13
FILE LAST UPDATED: 20 Sep 2004 (20040920/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 34 L3

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 7.08 163.97

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STRUCTURE FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2

h eb c g cg b cg eb

DICTIONARY FILE UPDATES: 20 SEP 2004 HIGHEST RN 748739-98-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L5 STR

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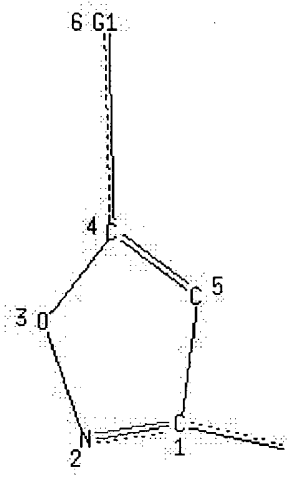
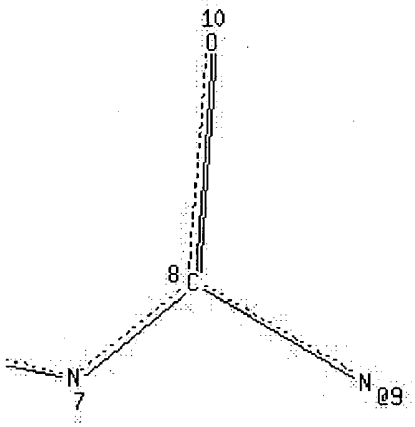
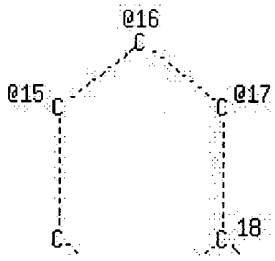
Cb 19Ak 20



Page 1-A





Page 1-B

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Page 1-C

Page 2-B
VAR G1=19/20
VAR G2=21/22
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NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 7 8 9 10 19 20 21 22
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 13
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

=> s 15
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SAMPLE SCREEN SEARCH COMPLETED - 19 TO ITERATE

100.0% PROCESSED 19 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 119 TO 641
PROJECTED ANSWERS: 8 TO 329

L6 8 SEA SSS SAM L5

=> s 15 full

h eb c g cg b cg eb

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THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 10:39:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    329 TO ITERATE

100.0% PROCESSED     329 ITERATIONS                          189 ANSWERS
SEARCH TIME: 00.00.01

L7          189 SEA SSS FUL L5

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   157.52     321.49

FILE 'HCAPLUS' ENTERED AT 10:39:55 ON 21 SEP 2004
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FILE COVERS 1907 - 21 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 20 Sep 2004  (20040920/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l7
L8          10 L7

=> s l8 and dumas, j?/au
          677 DUMAS, J?/AU
L9          3 L8 AND DUMAS, J?/AU

=> d l9, ibib abs fhitstr, 1-3

L9   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Cited References

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ACCESSION NUMBER:        2004:51821  HCAPLUS
DOCUMENT NUMBER:         140:296858
TITLE:                   Omega-carboxypyridyl substituted ureas as Raf kinase
                         inhibitors: SAR of the amide substituent
AUTHOR(S):               Khire, Uday R.; Bankston, Donald; Barbosa, James;
                         Brittelli, David R.; Caringal, Yolanda; Carlson,
                         Robert; Dumas, Jacques; Gane, Todd; Heald, Sarah L.;
                         Hibner, Barbara; Johnson, Jeffrey S.; Katz, Michael
                         E.; Kennure, Nancy; Kingery-Wood, Jill; Lee, Wendy;
                         Liu, Xiao-Gao; Lowinger, Timothy B.; McAlexander, Ian;
```

h eb c g cg b cg eb

Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Riedl, Bernd; Rong, Hong; Sibley, Robert N.; Smith, Roger A.; Wolanin, Donald

CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 783-786
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

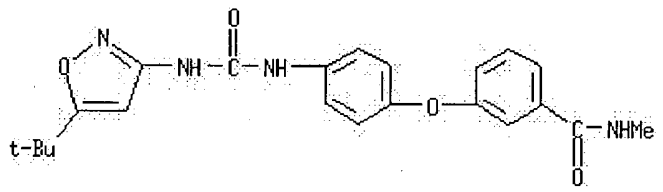
LANGUAGE: English

AB Bis-aryl ureas have been disclosed previously as a potent class of Raf kinase inhibitors. Modifications in the amide portion led to an improvement in aq. soly., an important characteristic for an oral drug. Based on this finding, we hypothesize that this portion of the mol. is directed towards the solvent in Raf-1.

IT **228999-58-4**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(structure and Raf kinase inhibitor activity of amide substituent of omega-carboxypyridyl substituted ureas)

RN 228999-58-4 HCAPLUS

CN Benzamide, 3-[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]phenoxy]-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425745 HCAPLUS

DOCUMENT NUMBER: 131:87909

TITLE: Inhibition of p38 kinase activity using substituted heterocyclic ureas

INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932111	A1	19990701	WO 1998-US26080	19981222

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,

h eb c g cg b cg eb

MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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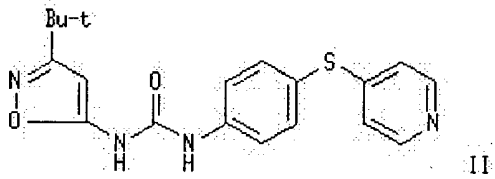
AU 739642	B2	20011018		
EP 1041982	A1	20001011	EP 1998-964709	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526223	T2	20011218	JP 2000-525102	19981222

PRIORITY APPLN. INFO.:
US 1997-995750 A 19971222
WO 1998-US26080 W 19981222

OTHER SOURCE(S): MARPAT 131:87909
GI

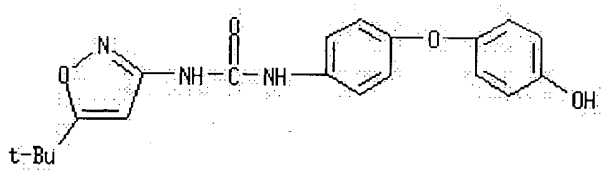


II

AB A method for treatment of p38-mediated disease other than cancer comprises administration of ANHCONHB [I; A = substituted isoxazolyl, pyrazolyl, thienyl, furyl; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-(4-pyridinylthio)aniline with 3-tert-butyl-5-isoxazolyl isocyanate in toluene gave title compd. II. In an in vitro p38 kinase assay, I displayed IC50 values of 1-10 μM.

IT **228999-08-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted heterocyclic ureas for treatment of p38 kinase-mediated diseases other than cancer)

RN 228999-08-4 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:425740 HCAPLUS

h eb c g cg b cg eb

DOCUMENT NUMBER: 131:73648
TITLE: Inhibition of raf kinase using substituted heterocyclic ureas
INVENTOR(S): **Dumas, Jacques**; Khire, Uday; Lowinger, Timothy Bruno; Paulsen, Holger; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Hatoum-Mokdad, Holia; Johnson, Jeffrey; Lee, Wendy; Redman, Aniko
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932106	A1	19990701	WO 1998-US26078	19981222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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EP 1047418	A1	20001102	EP 1998-965981	19981222
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JP 2001526220	T2	20011218	JP 2000-525097	19981222
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			WO 1998-US26078 W	19981222

OTHER SOURCE(S): MARPAT 131:73648
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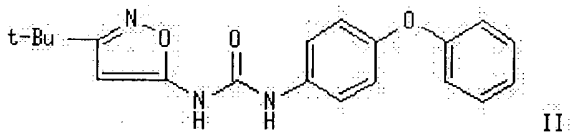


II

AB A method for treatment of cancerous cell growth mediated by raf kinase comprises administration of urea derivs. ANHCONHB [I; A = substituted isoxazolyl, thienyl, thiadiazolyl, furyl, pyrazolyl, etc.; B = (substituted) mono-, di-, or tricyclic aryl, heteroaryl contg. ≥1 5-6 membered arom. structure contg. 0-4 N, O, or S atoms]. Reaction of 4-phenyloxyphenyl isocyanate with 5-amino-3-tert-butylisoxazole in methylene chloride and heating at reflux temp. for 2 days gave title compd. II. In an in vitro raf kinase assay, I displayed IC50 values of 1-10 μM.

h eb c g cg b cg eb

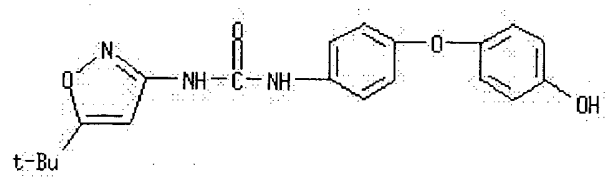
IT **228999-08-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of substituted heterocyclic ureas for treatment of cancerous cell growth mediated by raf kinase)

RN 228999-08-4 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 377 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 10:34:46 ON 21 SEP 2004
L4 34 S L3

FILE 'REGISTRY' ENTERED AT 10:36:32 ON 21 SEP 2004
L5 STRUCTURE UPLOADED
L6 8 S L5
L7 189 S L5 FULL

FILE 'HCAPLUS' ENTERED AT 10:39:55 ON 21 SEP 2004
L8 10 S L7
L9 3 S L8 AND DUMAS, J?/AU

=> s l8 not l9
L10 7 L8 NOT L9

=> s l10 and khire, u?/au
41 KHIRE, U?/AU
L11 0 L10 AND KHIRE, U?/AU

=> s l10 and lowinger, t?/au
44 LOWINGER, T?/AU
L12 1 L10 AND LOWINGER, T?/AU

=> d l12, ibib abs fhitstr, 1

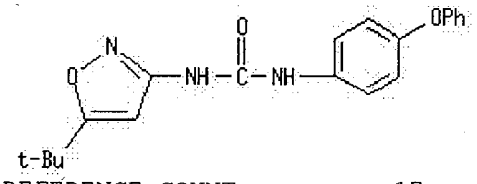
L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Other References

ACCESSION NUMBER: 2001:746592 HCAPLUS

h eb c g cg b cg eb

DOCUMENT NUMBER: 136:95577
TITLE: Discovery of heterocyclic ureas as a new class of raf kinase inhibitors: identification of a second generation lead by a combinatorial chemistry approach
AUTHOR(S): Smith, R. A.; Barbosa, J.; Blum, C. L.; Bobko, M. A.; Caringal, Y. V.; Dally, R.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; **Lowinger, T. B.**; Lyons, J.; Marsh, V.; Rogers, D. H.; Swartz, S.; Walling, T.; Wild, H.
CORPORATE SOURCE: Department of Chemistry Research, Bayer Research Center, West Haven, CT, 06516, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(20), 2775-2778
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heterocyclic ureas, such as N-3-thienyl N'-aryl ureas, have been identified as novel inhibitors of raf kinase, a key mediator in the ras signal transduction pathway. Structure-activity relationships were established, and the potency of the screening hit was improved 10-fold to IC50=1.7 μM. A combinatorial synthesis approach enabled the identification of a breakthrough lead (IC50=0.54 μM) for a second generation series of heterocyclic urea raf kinase inhibitors.
IT **228998-90-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic ureas as raf kinase inhibitors)
RN 228998-90-1 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 377 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 10:34:46 ON 21 SEP 2004
L4 34 S L3

FILE 'REGISTRY' ENTERED AT 10:36:32 ON 21 SEP 2004
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L6 8 S L5

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L7          189 S L5 FULL

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L10           7 S L8 NOT L9
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L12           1 S L10 AND LOWINGER, T?/AU

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L6           8 S L5
L7         189 S L5 FULL

     FILE 'HCAPLUS' ENTERED AT 10:39:55 ON 21 SEP 2004
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L13  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:          2004:589418  HCAPLUS
DOCUMENT NUMBER:           141:117198
TITLE:                     Therapeutic agent for wet age-related macular
                           degeneration
INVENTOR(S):               Matsuno, Kiyoshi; Koyama, Shinji
PATENT ASSIGNEE(S):        Santen Pharmaceutical Co., Ltd., Japan; Kirin Beer
                           Kabushiki Kaisha
SOURCE:                    PCT Int. Appl., 21 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:             Patent
LANGUAGE:                  Japanese
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
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     WO 2004060373          A1    20040722    WO 2003-JP16854          20031226
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2004217649 A2 20040805 JP 2003-431849 20031226

PRIORITY APPLN. INFO.: JP 2002-379857 A 20021227

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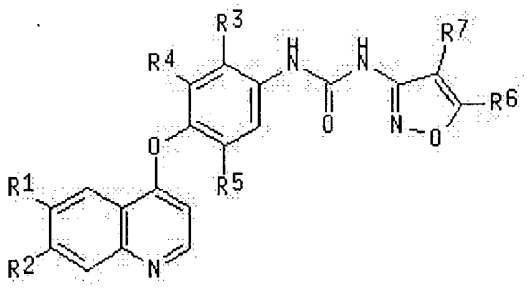

I

AB A therapeutic agent for wet age-related macular degeneration which contains as an active ingredient an N-quinolyloxyphenyl-N'-isoxazolylurea deriv. represented by the general formula (I; wherein R1 and R2 each is C1-6 alkoxy; R3 is halogeno; R4 and R5 each is hydrogen, halogeno, etc.; and R6 and R7 each is hydrogen, halogeno, C1-4 alkyl, etc.). The compd. has excellent choroidal angiogenesis inhibitory activity and is useful in treatments for wet age-related macular degeneration.

IT **475108-18-0**, N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-quinolyloxyphenyl-N'-isoxazolylurea derivs. as therapeutic agents for wet age-related macular degeneration)

RN 475108-18-0 HCAPLUS

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)

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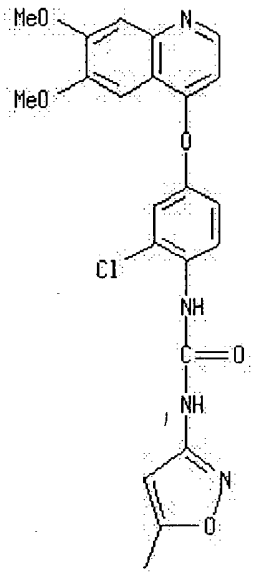
PAGE 1-A



PAGE 2-A

L13 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | More References

ACCESSION NUMBER: 2004:354935 HCAPLUS
DOCUMENT NUMBER: 140:363009
TITLE: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea salt crystals
INVENTOR(S): Matsunaga, Naoki; Yoshida, Satoshi; Yoshino, Ayako; Nakajima, Tatsuo
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035572	A1	20040429	WO 2003-JP13439	20031021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-306101 A 20021021

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AB This invention provides crystals of pharmaceutically acceptable salts of N-[2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea. The salt crystals are used in treating a disease selected from the group consisting of tumor, diabetic retinopathy, rheumatoid arthritis, psoriasis, atheroma arteriosclerosis, Kaposi's sarcoma and exudative age-related macular degeneration. The salt crystals have properties appropriate for prepns. for oral administration.

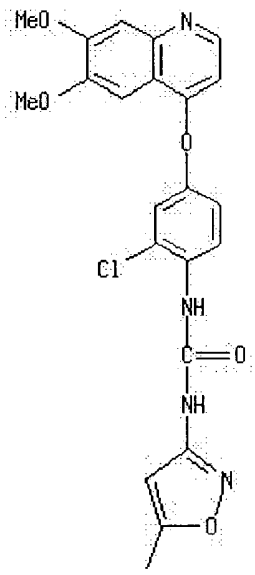
IT **682745-43-3P**

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea salt crystals with activity against tumor, diabetic retinopathy, rheumatoid arthritis, psoriasis, neovascularization, etc.)

RN 682745-43-3 HCAPLUS

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:182368 HCAPLUS
DOCUMENT NUMBER: 140:229401
TITLE: Three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands
INVENTOR(S): Come, Jon H.; Becker, Frank; Kley, Nikolai A.; Reichel, Christoph

h eb c g cg b cg eb

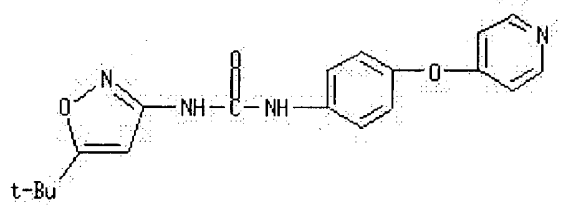
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S. Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004043388	A1	20040304	US 2002-234985		20020903
US 2003165873	A1	20030904	US 2002-91177		20020304
PRIORITY APPLN. INFO.:			US 2001-272932P	P	20010302
			US 2001-278233P	P	20010323
			US 2001-329437P	P	20011015
			US 2002-91177	A2	20020304

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Prepn. of compds., e.g a methotrexate moiety linked by a polyethylene gycol moiety to dexamethasone, is described.

IT **228999-48-2D**, conjugates
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

RN 228999-48-2 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-3-isoxazolyl]-N'-[4-(4-pyridinyloxy)phenyl]- (9CI) (CA INDEX NAME)



L13 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2002:849617 HCAPLUS
DOCUMENT NUMBER: 137:370101
TITLE: Preparation of quinoline derivatives having azolyl group and quinazoline derivatives as antitumor agents
INVENTOR(S): Kubo, Kazuo; Sakai, Teruyuki; Nagao, Rika; Fujiwara, Yasunari; Isoe, Toshiyuki; Hasegawa, Kazumasa
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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WO 2002088110	A1	20021107	WO 2002-JP4279		20020426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
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JP 2003012668	A2	20030115	JP 2002-126869		20020426
US 2003087907	A1	20030508	US 2002-132473		20020426
EP 1382604	A1	20040121	EP 2002-724651		20020426
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BR 2002009216	A	20040706	BR 2002-9216		20020426
NO 2003004595	A	20031219	NO 2003-4595		20031014
JP 2004224800	A2	20040812	JP 2004-101164		20040330
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			WO 2002-JP4279	W	20020426

OTHER SOURCE(S): MARPAT 137:370101

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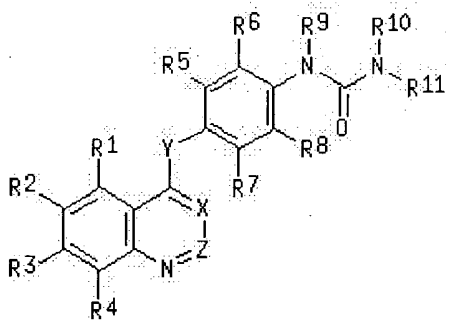

I

AB N-[(4-quinolinyl or 4-quinazolinyl)thio or -oxy]phenyl-N'-azolylurea derivs. represented by the formula (I) or pharmaceutically acceptable salts or solvates thereof [wherein X, Z = CH, N; Y = O, S; R1, R2, R3 = H, NO2, NH2, each (un)substituted C1-6 alkyl or alkoxy or C2-6 alkenyl or alkynyl; R4 = H; R5-R8 = H, halo, C1-4 alkyl, alkoxy, or alkylthio, CF3, NO2, NH2; R9, R10 = C1-6 alkyl, each (un)substituted C1-4 alkylcarbonyl or C1-6 alkyl; R11 = (un)substituted azolyl] are prepd. These compds. are useful for the treatment of tumor, diabetic retinopathy, chronic articular rheumatism, psoriasis, atherosclerosis , and Kaposi's sarcoma. They are also used for inhibiting neovascularization of a target blood vessel by contacting them with vascular endothelial cells of the target blood vessel. Thus, 100 mg 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline was dissolved in 5 mL CHCl3 and 0.5 mL Et3N, treated with a soln. of 100 mg triphosgene in CHCl3, and stirred at room temp. for 15 min, followed by adding 49 mg 2-aminothiazole, and the resulting mixt. was stirred at room temp. overnight to give 31 mg N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N;-(1,3-thiazol-2-yl)urea (II). II at 20 mg/kg/day for 9 days inhibited the growth of human lung cancer transplanted in nude mice by 92.0%. The compds. I in vitro showed IC50 of 0.001-0.0697 μM for inhibiting the phosphorylation of

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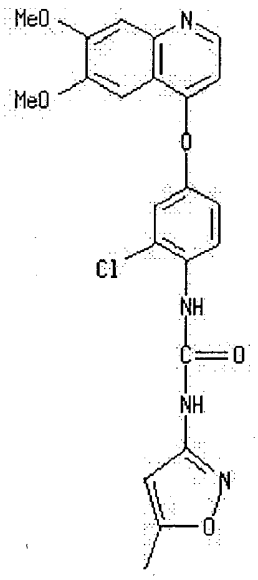
the intracellular domain of human vascular endothelial cell growth factor (VEGF) receptor KDR (kinase insert domain-contg. receptor) in IH3T3 cell expressing human KDR.

IT **475108-18-0P**, N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[(4-quinolinyl or 4-quinazolinyl)oxy]phenyl-N'-azolylurea derivs. as neovascularization inhibitors for treatment of tumor, diabetic retinopathy, chronic articular rheumatism, psoriasis, atherosclerosis, and Kaposi's sarcoma)

RN 475108-18-0 HCAPLUS

CN Urea, N-[2-chloro-4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:428885 HCAPLUS
DOCUMENT NUMBER: 137:6179
TITLE: Preparation of benzimidazoles as TIE-2 and/or VEGFR2 inhibitors
INVENTOR(S): Cheung, Mui; Harris, Philip Anthony; Hasegawa, Masaichi; Ida, Satoru; Kano, Kazuya; Nishigaki, Naohiko; Sato, Hideyuki; Veal, James Martin; Washio, Yoshiaki; West, Rob I.
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Glaxosmithkline K.K.
SOURCE: PCT Int. Appl., 217 pp.

h eb c g cg b cg eb

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044156	A2	20020606	WO 2001-US44553	20011128
WO 2002044156	A3	20021017		
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EP 1341771	A2	20030910	EP 2001-991963	20011128
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JP 2004517080	T2	20040610	JP 2002-546526	20011128
US 2004082583	A1	20040429	US 2003-433128	20031112
PRIORITY APPLN. INFO.:			US 2000-253868P P	20001129
			US 2001-310939P P	20010808
			WO 2001-US44553 W	20011128

OTHER SOURCE(S): MARPAT 137:6179
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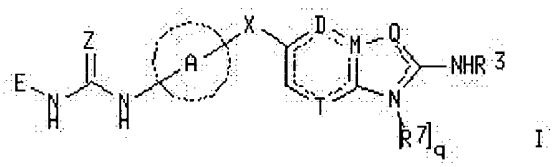

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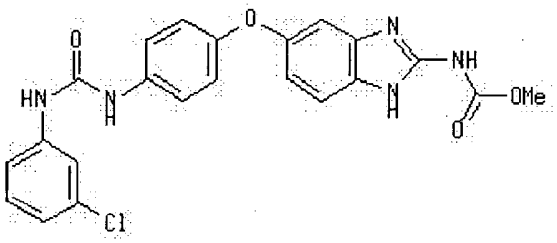

II

AB The title compds. [I; E = (un)substituted aryl, heteroaryl; A = aryl, heteroaryl, heterocyclyl; X = S, O, SO2, SO, CH2, CHOH, CO; Z = O, S; p = 0-1; q = 0-1; D = CH, T = CR8, M = C and Q = NT7p, wherein p = 0 and q = 1; or D = CH, T = CR8, M = C and Q = NR7p, wherein p =1 and q = 0, or D = CH, T = CR8, M = C and Q = S or O, wherein q = 0; or D = N, T = CR8, M = C and Q = NR7p, wherein either p or q = 0 and the other = 1; or D = CH, T = N, M = C and Q = NR7p, wherein either p or q = 0 and the other = 1; or D = CH, T = CR8, M = N and Q = CH, wherein q = 0; R1 = alkyl, haloalkyl, aryl, etc.; R2 = H, alkyl, aryl, etc.; R3 = alkylene or alkylene substituted by oxo, and is linked together with N atom to which it is attached and to one

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of the benzimidazole N atoms to form a heterocyclic compd. fused to the benzimidazole; R7 = H, alkyl, etc.; R8 = H, halo] and their salts, useful in the treatment of hyperproliferative diseases, were prepd. Thus, reacting Me [5-(4-aminophenoxy)-1H-benzimidazol-2-yl]carbamate (prepn. given) with 3-chlorophenyl isocyanate in THF afforded 69% II which showed pIC50 of > 7.0 in TIE-2 and VEGFR2 enzyme assays.

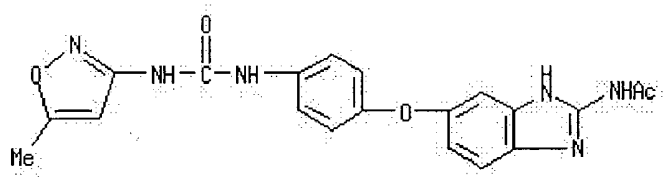
IT **433225-41-3P**

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(prepn. of benzimidazoles as TIE-2 and/or VEGFR2 inhibitors)

RN 433225-41-3 HCAPLUS

CN Acetamide, N-[5-[4-[[[(5-methyl-3-isoxazolyl)amino]carbonyl]amino]phenoxy]-1H-benzimidazol-2-yl]- (9CI) (CA INDEX NAME)



L13 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:314913 HCAPLUS
DOCUMENT NUMBER: 136:340689
TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis
INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki, Yasuyuki; Arimoto, Itaru
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 699 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032872	A1	20020425	WO 2001-JP9221	20011019
WO 2002032872	C1	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001095986	A5	20020429	AU 2001-95986	20011019

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EP 1415987 A1 20040506 EP 2001-976786 20011019
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NO 2003001731 A 20030619 NO 2003-1731 20030414
US 2004053908 A1 20040318 US 2003-420466 20030418
PRIORITY APPLN. INFO.: JP 2000-320420 A 20001020
JP 2000-386195 A 20001220
JP 2001-46685 A 20010222
WO 2001-JP9221 W 20011019
OTHER SOURCE(S): MARPAT 136:340689
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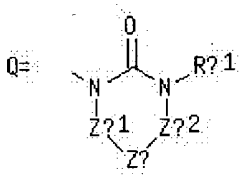

AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliph. hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepd. These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to soln. of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temp. for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT **417714-38-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

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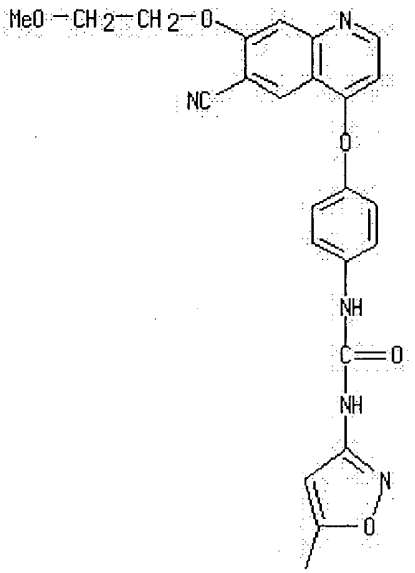
(prepn. of urea derivs. contg. nitrogenous arom. ring compds. as angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-38-6 HCAPLUS

CN Urea, N-[4-[[6-cyano-7-(2-methoxyethoxy)-4-quinolinyl]oxy]phenyl]-N'-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

Me

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L12            1 S L10 AND LOWINGER, T?/AU
L13            6 S L10 NOT L12
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